PROJECT REPORT
COMMITTEE ON FOOD RESEARCH
U. S. QUARTERMASTER FOOD AND CONTAINER INSTITUTE
FOR THE ARMED FORCES
CHICAGO ILLINOIS

RESEARCH AND DEVELOPMENT BRANCH
MILITARY PLANNING DIVISION
OFFICE OF THE
QUARTERMASTER GENERAL

COOPERATING INSTITUTION: Emory W. Thurston Laboratories	LOCALITY: Los Angeles, California
DIVISION: Research	DEPARTMENT:
OFFICIAL INVESTIGATOR: B. H. Ershoff	COLLABORATORS: Walter Marx
REPORT NO.: 8	FILE NO.: N-1105 — CONTRACT NO.: W11-009-qm-70168
FOR PERIOD COVERING: Sept., 1947 - December, 1947	INITIATION DATE: July 1, 1946

TITLE: [ ] PROGRESS REPORT [X] PHASE REPORT [ ] ANNUAL REPORT [ ] TERMINATION REPORT

"Effect of Stress Factors on Nutrition"

SUMMARY

Effects of Cholesterol Feeding on the Length of Survival of Immature Rats Fed Toxic Doses of Thyroid

Available data indicate that the length of survival of immature rats fed toxic levels of thyroid is significantly less than that observed in animals fed similar rations with thyroid omitted. A number of early deaths occur under conditions of thyroid feeding, with the immediate cause of death apparently heart failure[1]. Previous work indicates that yeast and desiccated whole liver will significantly prolong survival of immature rats fed toxic doses of thyroid[1-4]. It is the purpose of the present communication to report that cholesterol is similarly effective in prolonging survival of thyroid-fed rats.

Procedure and Results

Five experimental diets were employed in the present experiment (table 1.) Diets A and B were synthetic rations containing 0.5 per cent of desiccated thyroid and differing only in their content of cholesterol. Diets C and D were similar to diet A but contained 10 per cent yeast or desiccated whole liver, added in place of an equal amount of sucrose. Diet E was a control ration, similar to diet A but with thyroid omitted and replaced by sucrose. Fifty-six female rats of the Long-Evans strain were weaned at 21 to 23 days of age and litter mates divided as far as possible among the experimental groups listed in table 1. Animals were kept in metal cages with raised screen bottoms to prevent access to feces, and sufficient food was administered to assure ad

continued

RESEARCH AND DEVELOPMENT BRANCH MILITARY PLANNING DIVISION OFFICE OF THE QUARTERMASTER GENERAL	PROJECT REPORT COMMITTEE ON FOOD RESEARCH QUARTERMASTER FOOD AND CONTAINER INSTITUTE FOR THE ARMED FORCES CHICAGO ILLINOIS

COOPERATING INSTITUTION Emory W. Thurston Laboratories	LOCALITY Los Angeles, California	
DIVISION Research	DEPARTMENT	
OFFICIAL INVESTIGATOR B. H. Ershoff	COLLABORATORS Walter Marx	
REPORT NO. 8	FILE NO. N-1105	CONTRACT NO. W11-009-qm-7016
FOR PERIOD COVERING Sept., 1947 - December, 1947	INITIATION DATE July 1, 1946	

TITLE: [ ] PROGRESS REPORT [x] PHASE REPORT [ ] ANNUAL REPORT [ ] TERMINATION REPORT

"Effect of Stress Factors on Nutrition"

SUMMARY

Effects of Cholesterol Feeding on the Length of Survival of Immature Rats Fed Toxic Doses of Thyroid

Available data indicate that the length of survival of immature rats fed toxic levels of thyroid is significantly less than that observed in animals fed similar rations with thyroid omitted. A number of early deaths occur under conditions of thyroid feeding, with the immediate cause of death apparently heart failure[1]. Previous work indicates that yeast and desiccated whole liver will significantly prolong survival of immature rats fed toxic doses of thyroid[1-4]. It is the purpose of the present communication to report that cholesterol is similarly effective in prolonging survival of thyroid-fed rats.

Procedure and Results

Five experimental diets were employed in the present experiment (table 1.) Diets A and B were synthetic rations containing 0.5 per cent of desiccated thyroid and differing only in their content of cholesterol. Diets C and D were similar to diet A but contained 10 per cent yeast or desiccated whole liver, added in place of an equal amount of sucrose. Diet E was a control ration, similar to diet A but with thyroid omitted and replaced by sucrose. Fifty-six female rats of the Long-Evans strain were weaned at 21 to 23 days of age and litter mates divided as far as possible among the experimental groups listed in table 1. Animals were kept in metal cages with raised screen bottoms to prevent access to feces, and sufficient food was administered to assure ad

continued

lib feeding. Feeding was continued for 100 days or until death, whichever occurred sooner.

(Table I at end of paper)

Results are summarized in Table II. In agreement with earlier findings[1-4] the mortality rate of thyroid-fed rats was significantly greater on the synthetic ration (diet A) than on purified rations containing yeast or desiccated whole liver (diets C and D.) Cholesterol, however, was as effective as yeast or desiccated whole liver in prolonging survival of immature thyroid-fed rats. The average length of survival on diets containing cholesterol, yeast or desiccated whole liver was more than twice that which occurred on diet A (table II.) All rats fed the thyroid-free ration (diet E) survived the experimental period of 100 days. No significant differences were observed between animals fed the cholesterol and yeast-containing rations (diets B and C.) Gross appearance, gain in body weight and average length of survival were similar on both diets. Animals fed desiccated whole liver, in agreement with earlier findings[2-4], gained significantly more weight, however, than those on other thyroid-containing rations.

(Table II at end of paper)

Discussion

Recently Hoffmann and Hoffmann[7] have suggested that many of the toxic effects observed during hyperthyroidism may be due to excessive amounts of lysolecithin, a breakdown product of phospholipids, which is produced in increased amounts during this condition. Various sterols such as cholesterol and the steroid hormones of the adrenals are believed under normal conditions to neutralize the toxic effects of lysolecithin. Under conditions of prolonged thyroid feeding or during hyperthyroidism, however, the sterol reserves of the body may become exhausted with the result that toxic symptoms become manifest. If the above theory is correct increasing the cholesterol content of the diet might be expected to counteract, at least in part, the toxic effects of thyroid-feeding in the rat.

Findings in the present experiment indicate that cholesterol feeding prolonged significantly the average length of survival of immature rats fed toxic doses of thyroid. In this regard its action was similar to that obtained on diets containing desiccated whole liver or yeast. It differed from the liver-containing ration, however, in that it did not counteract the retardation of growth following thyroid-feeding in the immature rat. These findings are in agreement with those reported by Marx et al[8] concerning the anti-thyroid effects of cholesterol in the immature rat.

The beneficial effects of yeast or desiccated whole liver in prolonging survival of immature rats fed toxic doses of thyroid do not appear to be due to the steroid content of these foods.

Unpublished work from this laboratory [9] indicates that the survival-prolonging factor is present in the fat-free water-insoluble portion of desiccated whole liver, and that whole liver fat has virtually no activity in this regard. It is not unlikely, however, that the beneficial effects of yeast or desiccated whole liver on survival of immature rats fed toxic doses of thyroid may be due, at least in part, to the possible effect of these substances on steroid synthesis or utilization in the hyperthyroid rat.

Summary

Oral administration of cholesterol prolonged significantly the length of survival of immature rats fed toxic doses of thyroid.

Literature Cited

1. Ershoff, B.H., and Hershberg, D., Am. J. Physiol., 1945, 145, 16

2. Ershoff, B. H., Proc. Soc. Exp. Biol. and Med., 1947, 64, 500

3. Ershoff, B. H., Arch. Biochem., 1947, 15, 365

4. Betheil, J.J., Wiebelhaus, V.D., and Lardy, H.A., J. Nutrition, 1947, 34, 431

5. Sure, B., J. Nutrition, 1941, 22, 499

6. Drill, V.A., and Overman; R., Am. J. Physiol.,1942, 135, 474

7. Hoffmann, F., and Hoffmann, E.J. de, Public. del instit. fisiol., Universidad de Chile, 1943

8. Marx, Walter, et al. In press

9. Ershoff, B. H., in preparation.

Table 1

Composition of experimental diets

Dietary component	Diet A	Diet B	Diet C	Diet D	Diet E
Thyroid[1]	0.5	0.5	0.5	0.5	0.0
Cholesterol[1]	0.0	1.0	0.0	0.0	0.0
Yeast[1]	0.0	0.0	10.0	0.0	0.0
Liver[1]	0.0	0.0	0.0	10.0	0.0
Casein[1]	22.0	22.0	22.0	22.0	22.0
Salt Mixture[2]	4.5	4.5	4.5	4.5	4.5
Sucrose	73.0	72.0	63.0	63.0	73.5

To each kg of the above diets were added the following synthetic vitamins: thiamine hydrochloride 72 mg, riboflavin 9 mg, pyridoxine hydrochloride 15 mg, calcium pantothenate 67.2 mg, nicotinic acid 60 mg, 2-methyl-naphthoquinone 5 mg and choline chloride 1.2 g[3]. Each rat also received 3 times weekly the following supplement: cottonseed oil (Wesson) 500 mg, alpha-tocopherol 1 mg, and a vitamin A-D concentrate[4] containing 50 U.S.P. units of vitamin A and 5 U.S.P. units of vitamin D.

Footnotes to Table 1

1. Dietary ingredients were obtained from the following sources: Thyroid Powder, U.S.P., Amour and Co., Chicago, Ill. Cholesterol, Technical, National Oil Products Co., Harrison, N.J. Brewer's Type Yeast No. 200, Anheuser-Busch, Inc., St. Louis, Mo. Whole Dried Liver Powder, Amour and Co., Chicago Ill. Vitamin Test Casein, General Biochemicals, Inc., Chagrin Falls, Ohio.
2. Sure's Salt Mixture No. 1[5].
3. In view of the increased requirements for thiamine, pyridoxine and pantothenic acid in the hyperthyroid rat[6], the B vitamins in the present experiment were administered in excessive amounts in order to assure an adequacy of these factors in the diet.
4. Nopco Fish Oil Concentrate, assaying 800,000 U.S.P. units of vitamin A and 80,000 U.S.P. units of vitamin D per gram.

continued

Table II

Summary of experimental data

Dietary group	Number of animals	Initial body weight	Average gain in body weight on following days of the experiment: 28th	60th	100th	Per cent surviving[1]	Average survival time[1,2]
		g.	g.	g.	g.		days
A	20	43.6	43.4 (10)	83.0 (2)	--	0.0	34.3 ± 5.2
B	10	42.7	53.0 (9)	90.4 (5)	103.4 (5)	50.0	70.6 ± 9.8
C	10	43.1	66.8 (8)	87.4 (6)	101.8 (5)	50.0	73.5 ± 8.8
D	10	42.9	98.4 (8)	147.7 (6)	168.3 (6)	60.0	76.2 ± 9.2
E	6	43.1	100.6 (6)	151.2 (6)	173.5 (6)	100.0	100.0 ± 0.0

The values in parentheses indicate the number of animals which survived of which this is an average.

Footnotes to Table II

1. Experimental period - 100 days
2. Averages were computed on the basis of a 100 day survival time for animals alive at the termination of the experiment.
3. Including standard error of the mean calculated as follows:

$\sqrt{\frac{\Sigma d^2}{n}} \Big/ \sqrt{n}$ where "d" is the deviation from the mean and "n" is the number of observations.